Summary:
Based on critical review of the literature listed below, the Canine Cutaneous Mast Cell Tumor Subgroup has concluded and recommends the following regarding grading for canine cutaneous mast cell tumors.

Conclusions:

1. The Patnaik system has been the ‘gold’ standard and has provided a strong foundation in the grading of canine cutaneous mast cell tumors. However, as certain criteria within the grading system are unclear and require subjective interpretation, significant uncertainty and inter-pathologist variability exists. This has presented challenges for clinicians in determining clinical behavior from tumor grade and thus the need for adjuvant therapy, especially for “grade II” mast cell tumors (see point #4).

2. The Kiupel 2-tier system has merit; however, it also contains poorly defined, subjective criteria (“bizarre” nuclei, karyomegaly), which may continue to create inter-pathologist variability similar to that which has plagued the Patnaik scheme. From a clinical perspective, the 2-tier system may make clinical decisions similarly challenging for “low grade” mast cell tumors as those faced for Patnaik “Grade II” mast cell tumors. Additionally, with almost no therapeutic literature predicated on this grading scheme to date, it is difficult to relate low vs. high grade to chemotherapy or radiation therapy findings in past studies. Further investigation is needed to validate the 2-tier system. Until such studies are done, it is premature to adopt the Kiupel 2-tier system as the sole standard reporting mechanism for canine cutaneous mast cell tumors.
3. Mitotic Index (MI) has significant prognostic value and is a more objective variable which mitigates inter-observer variability and has been validated with two studies. However, the prognostic cut-offs for MI vary between the studies and MI must be standardized as to the fields selected for counting and method of reporting.

4. Regardless of the grading system used, grade must be considered as only one prognostic factor and used in conjunction with the overall clinical picture: size and possibly site of the MCT, presence of metastases (stage), completeness and quality of surgical margins, prognostic markers, and new/emerging markers that have not yet been evaluated.

**Recommendations and future direction:**

1. Until additional studies are done to validate the 2-tier system, both the Patnaik system and the Kiupel 2-tier system should be reported for all canine cutaneous mast cell tumors. All diagnostic pathologists reporting on canine cutaneous MCTs should have the criteria for each respective system (as published) listed and readily available/accessible for reference at the time of grading. (See Appendix p. 4)

2. Mitotic Index should be reported in all cases and should be standardized as an absolute number: #MF/10 HPF (400X). Additionally, in adherence with evaluation methods used in both studies that demonstrated prognostic significance of MI, mitotic figures (MFs) should be counted in regions with the highest mitotic activity as determined initially on a low power scan of the specimen.

3. Further investigation into the value of prognostic markers (i.e. KIT, c-kit mutation, Ki67, AgNors, others still to be determined) as an adjunct to routine histopathology reporting of mast cell tumors is warranted.

**Literature Reviewed:**


Canine Cutaneous Mast Cell Tumor Grading Systems

Patnaik Grading Criteria, 1984

<table>
<thead>
<tr>
<th>Location</th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demis and interfollicular spaces</td>
<td>Infiltrate lower dermal and subcutaneous tissue, some extend to skeletal muscles or surrounding tissues</td>
<td>Replace subcutaneous and deep tissues</td>
<td></td>
</tr>
<tr>
<td>Cell morphology</td>
<td>Round, monomorphic, amelioration of cytoplasm with medium-sized granules</td>
<td>Round to ovoid, moderately pleomorphic, with scattered spindle and giant cells; most cells distinct cytoplasm with fine granules, but some with indistinct cytoplasm and large/hyperchromatic granules</td>
<td>Round, ovoid, or spindle shaped, pleomorphic, medium sized; cytoplasm indistinct with granules that are fine or not obvious; many giant cells and scattered multinucleated cells</td>
</tr>
<tr>
<td>Nuclear morphology</td>
<td>Round, condensed chromatin</td>
<td>Infiltrated with scattered chromatin and single nuclei; some with double nuclei</td>
<td>Indented to round vesiculated, with 1 or more prominent nuclei; common multinucleated cells</td>
</tr>
<tr>
<td>Architecture, cellularity, stromal reaction</td>
<td>Arranged in rows or small groups, separated by mature collagen fibers of the dermis</td>
<td>Moderately to highly cellular, arranged in groups with thin, fibrovascular stroma (sometimes thick and fibrocollagenous with areas of hyalinization)</td>
<td>Cellular, arranged in closely packed sheets; stroma fibrovascular or thick and fibrocollagenous with areas of hyalinization</td>
</tr>
<tr>
<td>Mitotic figures</td>
<td>None</td>
<td>Rare (0-2/high-power field)</td>
<td>Common (3-6/high-power field)</td>
</tr>
<tr>
<td>Edema and necrosis</td>
<td>Minimal</td>
<td>Areas of diffuse edema and necrosis</td>
<td>Edema, haemorrhage, and necrosis common</td>
</tr>
</tbody>
</table>

Two-Tier Grading Criteria, 2011

High-grade MCT is characterized by any one following criteria:

1. \( \geq 7 \) MFs/10hpf
   - Evaluated in regions with highest mitotic activity
2. \( \geq 3 \) multinucleated cells / 10hpfs
   - Where \( \geq 3 \) nuclei constitutes a multinucleated cell
3. \( \geq 3 \) bizarre nuclei / 10hpf
   - Highly atypical with marked indentations, segmentation, and irregular shape
4. Karyomegaly
   - Where at least 10% of neoplastic cells vary by 2-fold

References:

